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PDR® entry for

DILAUDID® (Abbott)
hydromorphone hydrochloride

Rx only

DESCRIPTION

DILAUDID (hydromorphone hydrochloride), a hydrogenated ketone of morphine, is a narcotic analgesic. It is available in:

Ampules (for parenteral administration) containing:

1 mg, 2 mg, and 4 mg hydromorphone hydrochloride per mL with 0.2% sodium citrate, 0.2% citric acid solution. DILAUDID ampules are sterile.

Multiple Dose Vials (for parenteral administration) containing:

20 mL of solution. Each mL contains 2 mg hydromorphone hydrochloride and 0.5 mg edetate disodium with 1.8 mg methylparaben and 0.2 mg propylparaben as preservatives. Sodium hydroxide or hydrochloric acid is used for pH adjustment. DILAUDID multiple dose vials are sterile.

Color Coded Tablets (for oral administration) containing:

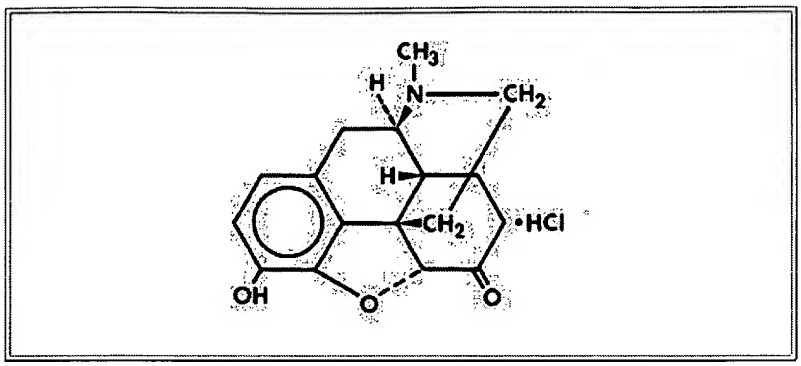
2 mg hydromorphone hydrochloride (orange tablet) and D&C red #30 Lake dye, D&C yellow #10 Lake dye, lactose, and magnesium stearate. 4 mg hydromorphone hydrochloride (yellow tablet) and D&C yellow #10 Lake dye, lactose, and magnesium stearate.

Suppositories (for rectal administration) containing:

3 mg hydromorphone hydrochloride in a cocoa butter base with silicon dioxide.

Non-Sterile Powder (for prescription compounding) containing hydromorphone hydrochloride.

The structural formula of DILAUDID (hydromorphone hydrochloride) is:



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CLINICAL PHARMACOLOGY

DILAUDID is a narcotic analgesic; its principal therapeutic effect is relief of pain. The precise mechanism of action of DILAUDID and other opiates is not known, although it is believed to relate to the existence of opiate receptors in the central nervous system. There is no intrinsic limit to the analgesic effect of DILAUDID; like morphine, adequate doses will relieve even the most severe pain. Clinically, however, dosage limitations are imposed by the adverse effects, primarily respiratory depression, nausea, and vomiting, which can result from high doses.

DILAUDID has diverse additional actions. It may produce drowsiness, changes in mood and mental clouding, depress the respiratory center and the cough center, stimulate the vomiting center, produce pinpoint constriction of the pupil, enhance parasympathetic activity, elevate cerebrospinal fluid pressure, increase biliary pressure, produce transient hyperglycemia.

Generally, the analgesic action of parenterally administered DILAUDID is apparent within 15 minutes and usually remains in effect for more than five hours. The onset of action of oral DILAUDID is somewhat slower, with measurable analgesia occurring within 30 minutes.

In human plasma the half-life of a DILAUDID 4 mg tablet is 2.6 hours. In a random crossover study in six subjects, 4 mg of oral DILAUDID produced a mean concentration/time curve similar to that of 2 mg DILAUDID I.V., after the first hour.

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INDICATIONS AND USAGE

DILAUDID is indicated for the relief of moderate to severe pain such as that due to:

Surgery

Cancer

Trauma (soft tissue & bone)

Biliary Colic

Myocardial Infarction

Burns

Renal Colic

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CONTRAINDICATIONS

DILAUDID is contraindicated in patients with a known hypersensitivity to hydromorphone; in the presence of an intracranial lesion associated with increased intracranial pressure; and whenever ventilatory function is depressed (chronic obstructive pulmonary disease, cor pulmonale, emphysema, kyphoscoliosis, status asthmaticus).

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WARNINGS

Respiratory Depression: DILAUDID produces dose-related respiratory depression by acting directly on brain stem respiratory centers. DILAUDID also affects centers that control respiratory rhythm, and may produce irregular and periodic breathing.

Head Injury and Increased Intracranial Pressure: The respiratory depressant effects of narcotics and their capacity to elevate cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions or a preexisting increase in intracranial pressure. Furthermore, narcotics produce effects which may obscure the clinical course of patients with head injuries.

Acute Abdominal Conditions: The administration of narcotics may obscure the diagnosis or clinical course of patients with acute abdominal conditions.

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PRECAUTIONS

Special Risk Patients: DILAUDID should be used with caution in elderly or debilitated patients and those with impaired renal or hepatic function, hypothyroidism, Addison's disease, prostatic hypertrophy or urethral stricture. As with any narcotic analgesic agent, the usual precautions should be observed and the possibility of respiratory depression should be kept in mind.

Cough Reflex: DILAUDID suppresses the cough reflex; as with all narcotics, caution should be exercised when DILAUDID is used postoperatively and in patients with pulmonary disease.

Usage in Ambulatory Patients: Narcotics may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks such as driving a car or operating machinery; patients should be cautioned accordingly.

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Drug Interactions: Patients receiving other narcotic analgesics, general anesthetics, phenothiazines, tranquilizers, sedative-hypnotics, tricyclic antidepressants or other CNS depressants (including alcohol) concomitantly with DILAUDID may exhibit an additive CNS depression. When such combined therapy is contemplated, the dose of one or both agents should be reduced.

Parenteral Administration: The parenteral form of DILAUDID may be given intravenously, but the injection should be given very slowly. Rapid intravenous injection of narcotic analgesics increases the possibility of side effects such as hypotension and respiratory depression.

Reports of mild to severe seizures and myoclonus have been reported in severely compromised patients, administered high doses of parenteral hydromorphone, for cancer and severe pain. Opioid administration at very high doses is associated with seizures and myoclonus in a variety of diseases where pain control is the primary focus.

Pregnancy: Pregnancy Category C. DILAUDID has been shown to be teratogenic in hamsters when given in doses 600 times the human dose. There are no adequate and well-controlled studies in pregnant women. DILAUDID should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nonteratogenic effects: Babies born to mothers who have been taking opioids regularly prior to delivery will be physically dependent. The withdrawal signs include irritability and excessive crying, tremors, hyperactive reflexes, increased respiratory rate, increased stools, sneezing, yawning, vomiting, and fever. The intensity of the syndrome does not always correlate with the duration of maternal opioid use or dose. There is no consensus on the best method of managing withdrawal. Chlorpromazine 0.7 to 1.0 mg/kg q6h, phenobarbital 2 mg/kg q6h, and paregoric 2 to 4 drops/kg q4h, have been used to treat withdrawal symptoms in infants. The duration of therapy is 4 to 28 days, with the dosages decreased as tolerated.

Labor and Delivery: As with all narcotics, administration of DILAUDID to the mother shortly before delivery may result in some degree of respiratory depression in the newborn, especially if higher doses are used.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from DILAUDID, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use: Safety and effectiveness in children have not been established.

Geriatric Use: Clinical studies of DILAUDID did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

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ADVERSE REACTIONS

Central Nervous System: Sedation, drowsiness, mental clouding, lethargy, impairment of mental and physical performance, anxiety, fear, dysphoria, dizziness, psychic dependence, mood changes.

Gastrointestinal System: Nausea and vomiting occur infrequently; they are more frequent in ambulatory than in recumbent patients. The antiemetic phenothiazines are useful in suppressing these effects; however, some phenothiazine derivatives seem to be antianalgesic and to increase the amount of narcotic required to produce pain relief, while other phenothiazines reduce the amount of narcotic required to produce a given level of analgesia. Prolonged administration of DILAUDID may produce constipation. Opiate agonist-induced increase in intraluminal pressure may endanger surgical anastomosis.

Cardiovascular System: Circulatory depression, peripheral circulatory collapse and cardiac arrest have occurred after rapid intravenous injection. Orthostatic hypotension and fainting may occur if a patient stands up suddenly after receiving an injection of DILAUDID.

Genitourinary System: Ureteral spasm, spasm of vesical sphincters and urinary retention have been reported.

Respiratory Depression: DILAUDID® (hydromorphone hydrochloride) produces dose-related respiratory depression by acting directly on brain stem respiratory centers. DILAUDID also affects centers that control respiratory rhythm, and may produce irregular and periodic breathing. If significant respiratory depression occurs, it may be antagonized by the use of naloxone hydrochloride. The usual adult dose of 0.4 to 0.8 mg given *intramuscularly or intravenously* , promptly reverses the effects of morphine-like opioid agonists such as DILAUDID. In patients who are physically dependent, small doses of naloxone may be sufficient not only to antagonize respiratory depression, but also to precipitate withdrawal phenomena. The dose of naloxone should therefore be adjusted accordingly in such patients. Since the duration of action of DILAUDID may exceed that of the

antagonist, the patient should be kept under continued surveillance; repeated doses of the antagonist may be required to maintain adequate respiration. Apply other supportive measures when indicated.

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DRUG ABUSE AND DEPENDENCE

DILAUDID is a Schedule II narcotic. Psychic dependence, physical dependence, and tolerance may develop upon repeated administration of narcotics; therefore, DILAUDID should be prescribed and administered with caution. However, psychic dependence is unlikely to develop when DILAUDID is used for a short time for the treatment of pain. Physical dependence, the condition in which continued administration of the drug is required to prevent the appearance of a withdrawal syndrome, usually assumes clinically significant proportions only after several weeks of continued narcotic use, although some mild degree of physical dependence may develop after a few days of narcotic therapy. Tolerance, in which increasingly large doses are required in order to produce the same degree of analgesia, is manifested initially by a shortened duration of analgesic effect, and subsequently by decreases in the intensity of analgesia. The rate of development of tolerance varies among patients.

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OVERDOSAGE

Signs and Symptoms: Serious overdosage with DILAUDID is characterized by respiratory depression (a decrease in respiratory rate and/or tidal volume, Cheyne-Stokes respiration, cyanosis), extreme somnolence progressing to stupor or coma, skeletal muscle flaccidity, cold and clammy skin, and sometimes bradycardia and hypotension. In severe overdosage, particularly by the intravenous route, apnea, circulatory collapse, cardiac arrest, and death may occur.

Treatment: Primary attention should be given to the reestablishment of adequate respiratory exchange through provision of a patent airway and institution of assisted or controlled ventilation. The narcotic antagonist naloxone hydrochloride is a specific antidote against respiratory depression which may result from overdosage or unusual sensitivity to narcotics, including DILAUDID. Therefore, naloxone hydrochloride should be administered as described under *Adverse Reactions* (see *Respiratory Depression*) in conjunction with ventilatory assistance.

Since the duration of action of DILAUDID may exceed that of the antagonist, the patient should be kept under continued surveillance; repeated doses of the antagonist may be required to maintain adequate respiration. An antagonist should not be administered in the absence of clinically significant respiratory or cardiovascular depression. Oxygen, intravenous fluids, vasopressors, and other supportive measures should be employed

as indicated.

In cases of overdosage with oral DILAUDID, gastric lavage or induced emesis may be useful in removing unabsorbed drug from conscious patients.

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DOSAGE AND ADMINISTRATION

Parenteral: The usual starting dose is 1-2 mg *subcutaneously* or *intramuscularly* every 4 to 6 hours as necessary for pain control. The dose should be adjusted according to the severity of pain, as well as the patient's underlying disease, age, and size. Patients with terminal cancer may be tolerant to narcotic analgesics and may, therefore, require higher doses for adequate pain relief. Intravenous or subcutaneous administration is usually not painful. Should intravenous administration be necessary, the injection should be given ***slowly*** , over at least 2 to 3 minutes, depending on the dose. A gradual increase in dose may be required if analgesia is inadequate, tolerance occurs, or if pain severity increases. The first sign of tolerance is usually a reduced duration of effect. NOTE: Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. A slight yellowish discoloration may develop in DILAUDID ampules and multiple dose vials. No loss of potency has been demonstrated.

Oral: The usual oral dose is 2 mg every 4 to 6 hours as necessary. The dose must be individually adjusted according to severity of pain, patient response and patient size. More severe pain may require 4 mg or more every 4 to 6 hours. If the pain increases in severity, analgesia is not adequate or tolerance occurs, a gradual increase in dosage may be required. If pain is exceedingly severe, or if prompt response is desired, parenteral DILAUDID should be used initially in adequate amounts to control the pain.

Rectal: DILAUDID suppositories (3 mg) may provide longer duration of relief which could obviate additional medication during the sleeping hours. The usual adult dose is one (1) suppository inserted rectally every 6 to 8 hours or as directed by physician.

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HOW SUPPLIED

Ampules: (One mL sterile solution for parenteral administration)

1 mg/mL ampules-Boxes of 10-NDC #0074-2332-11

2 mg/mL ampules-Boxes of 10-NDC #0074-2333-11
Boxes of 25-NDC #0074-2333-26

4 mg/mL ampules-Boxes of 10-NDC #0074-2334-11

Multiple D se Vials: (20 mL sterile solution for parenteral administration)

2 mg/mL-20 mL multiple dose vials-NDC #0074-2414-1

Cauti n: The packaging (vial stopper) of this product contains rubber latex which may cause allergic reactions.

Color Coded Tablets:

2 mg tablet (orange, debossed with the Abbott logo on one side and the number 2 on the opposite side)-

Bottles of 100-NDC #0074-2415-14

Abbo-Pac® Unit Dose Packages of 100 (4x25)- NDC #0074-2415-12

Bottles of 500-NDC #0074-2415-54

4mg tablet (yellow, debossed with the Abbott logo on one side and the number 4 on the opposite side)-

Bottles of 100-NDC #0074-2416-14

Abbo-Pac® Unit Dose Packages of 100 (4x25)- NDC #0074-2416-12

Bottles of 500-NDC #0074-2416-54

Rectal Suppositories: 3 mg suppositories-Boxes of 6-NDC #0074-2451-07.

Non-Sterile Powder: For prescription compounding.

15 grain vial-NDC #0074-2428-16

Storage: Parenteral and oral dosage forms of DILAUDID should be stored at 25°C (77°F); excursions permitted to 15°C-30°C (59°-86°F). [See USP Controlled Room Temperature]. Protect from light. DILAUDID suppositories should be stored in a refrigerator.

A Schedule CII Narcotic. DEA order form required.

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ABBOTT LABORATORIES

NORTH CHICAGO, IL 60064, U.S.A.

PRINTED IN U.S.A.

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PRODUCT PHOTO(S):

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